Safety Data Sheet

bis(Chloromethyl) ether

Division of Safety
National Institutes
of Health

WARNING!

THIS COMPOUND IS ACUTELY TOXIC (CAUSING SEVERE IRRITATION TO SKIN, EYES, MUCOUS MEMBRANES, AND LUNGS), CARCINOGENIC, AND MUTAGENIC. AVOID FORMATION AND BREATHING OF AEROSOLS OR VAPORS.

LABORATORY OPERATIONS SHOULD BE CONDUCTED IN A FUME HOOD, GLOVE BOX, OR VENTILATED CABINET.

AVOID SKIN CONTACT: IF EXPOSED, WASH WITH SOAP AND WATER.

FOR EYE EXPOSURE, IRRIGATE IMMEDIATELY WITH LARGE AMOUNTS OF WATER. FOR INGESTION, ADMINISTER AN ANTACID PREPARATION AND INDUCE VOMITING. FOR INHALATION, REMOVE VICTIM PROMPTLY TO CLEAN AIR. ADMINISTER RESCUE BREATHING IF NECESSARY. REFER TO PHYSICIAN.

IN CASE OF LABORATORY SPILL, WEAR PROTECTIVE CLOTHING DURING CLEANUP. AVOID SKIN CONTACT OR BREATHING OF AEROSOLS OR VAPORS. COVER SPILL WITH 1% AMMONIA SOLUTION. DISPOSE OF WASTE SOLUTIONS AND MATERIALS APPROPRIATELY.

A. Background

bis(Chloromethyl) ether (BCME) shows acute and chronic toxicity in experimental laboratory animals and in humans. BCME is a proven carcinogen in humans and in many species of laboratory animals. BCME is used in the laboratory as a research chemical and as an analytical standard.

B. Chemical and Physical Data

1. Chemical Abstract No.: 542-88-1

issued 10/82

2. Synonyms:

BCME	sym-Dichloro-dimethyl ether
BIS-CME	sym-Dichloromethyl ether
Chloro(chloromethoxy) methane	Dimethyl-1,1'-dichloroether
Chloromethyl ether	Methane, oxybis(chloro- (9CI)

3. Molecular formula: $C_2H_4Cl_2O$ structure: $Cl\text{-}CH_2\text{-}O\text{-}CH_2\text{-}Cl$

   weight: 114.96

4. Density: liquid: 1.328 g/cm^3 (15°C/4°C); vapor (air = 1): 4.0.

5. Absorption spectroscopy: The IR and NMR (Van Duuren et al., 1968), Raman (Katayama and Morino, 1949), and MS (Shadoff et al., 1973) spectra have been reported.

6. Volatility: Vapor pressure = 30 mm Hg at 22°C.

7. Solubility: Decomposes in water; soluble in alcohol, ether, acetone, and chloroform.

8. Description, appearance: Colorless, volatile liquid.

9. Boiling point: 104°C.

   Melting point: -41.5°C.

10. Stability: Unstable in aqueous solution, but fairly stable in moist air (Tou and Kallos, 1974).

11. Chemical reactivity: Decomposed by water and by aqueous and alcoholic alkali. Reacts with nucleophilic groups such as -OH, $-NH_2$, and -SH.

12. Flash point: Less than 19°C.

13. Autoignition temperature: No data.

14. Flammable limits: No data.

Fire, Explosion, and Reactivity Hazard Data

1. In case of fire, use extinguisher suited for the particular combustible material. Fire fighters should wear air-supplied respirators with full-face masks.

2. BCME is very volatile and it could cause a fire inside a glove box.

3. BCME decomposes in aqueous media.

4. Nucleophiles such as alcoholic hydroxyl, amino, and thiol compounds degrade BCME, but the reaction products would not be expected to cause any unusual hazards.

5. The hydrolysis products (hydrochloric acid and formaldehyde [known irritants]) do not present any unusual hazards.

6. To lessen the chance of accidental fire, any spark-producing equipment should be remote.

Operational Procedures

The NIH Guidelines for the Laboratory Use of Chemical Carcinogens describe operational practices to be followed when potentially carcinogenic chemicals are used in NIH laboratories. The Guidelines should be consulted to identify the proper use conditions required and specific controls to be implemented during normal and complex operations or manipulations involving BCME.

1. Chemical inactivation: No validated method has been reported. One percent ammonia solution has been reported to rapidly destroy BCME (Alvarez and Rosen, 1976).

2. Decontamination: Turn off equipment that could be affected by BCME or the materials used for cleanup. Call the NIH Fire Department (dial 116) for assistance. Wash surfaces with copious quantities of 1% ammonia solution. Glassware should be rinsed (in a hood) with water, followed by soap and water. Animal cages should be washed with water.

3. Disposal: No waste streams containing BCME shall be disposed of in sinks or general refuse. Surplus BCME or chemical waste streams contaminated with BCME shall be handled as hazardous chemical waste and disposed of in accordance with the NIH chemical waste disposal system. Nonchemical waste (e.g., animal carcasses and bedding) containing BCME shall be handled and packaged for incineration in accordance with the NIH medical-pathological waste disposal system. Potentially infectious waste (e.g., tissue cultures) containing BCME shall be packaged for incineration, as above. Burnable waste (e.g, absorbent bench top liners) minimally contaminated with BCME shall be handled as potentially infectious waste and packaged for incineration, as above. Absorbent materials (e.g., associated with spill cleanup) grossly contaminated shall be handled in accordance with the chemical waste disposal system. Radioactive waste containing BCME shall be handled in accordance with the NIH radioactive waste disposal system.

4. Storage: Store in ampoules or screw-capped bottles with Teflon or conical polyethylene cap liners at 0-5°C in an explosion-safe refrigerator.

Monitoring and Measurement Procedures Including Direct Field Measurements and Sampling for Subsequent Laboratory Analysis

1. Sampling: From air: (a) adsorption on polymeric beads (Pellizzari, 1974); (b) derivatization through impinger traps containing a derivatizing agent (Drew et al., 1975; Shadoff et al., 1973). From water: by use of a hollow fiber probe into the media to be analyzed and connected to an MS for analysis (Tou et al., 1974; Tou and Kallos, 1974; Westover et al., 1974).

2. Separation and analysis: BCME, after adsorption, is recovered by thermal elution. Several methods have been developed for the determination of BCME in air, such as high-resolution MS (Collier, 1972), GC-MS (Shadoff et al., 1973), derivative GC (Solomon and Kallos, 1975; Van de Ven and Vanema, 1979), GC-high-resolution MS (Evans et al., 1975), dual-column GC (Frankel and Black, 1976), and a nonspecific colorimetric procedure (Drew et al., 1975). The unequivocal characterization of BCME would require the use of more than one method.

Biological Effects (Animal and Human)

1. Absorption: Because of the high reactivity of BCME in water and biological media, it is virtually impossible to obtain absorption data, and none have been reported. However, the acute toxic effects suggest that BCME and/or its hydrolysis products are rapidly absorbed by inhalation, ingestion, and parenteral injection and through the skin.

2. Distribution: No data (for reasons mentioned above).

3. Metabolism and excretion: No data.

4. Toxic effects: The acute LD50s are 210 mg/kg (rat, oral) and 280 mg/kg (rabbit, percutaneous). Inhalation toxicity (LC50) is 7 ppm in the rat and hamster for a 7-hour exposure and 25 mg/m^3 in the mouse for a 6-hour exposure. This indicates a considerably higher toxicity for BCME than for chloromethyl methyl ether. BCME is an established human carcinogen (Althouse et al., 1980). Accidental exposure to high concentrations, involving both inhalation of vapors and direct skin contact with BCME, results in second and third degree skin burns, burns of the mucous membranes of the upper respiratory tract, eye irritation, corneal injury, atrophy of the optic nerve, pneumonia, and fibrosis of the lungs, leading to death. With less severe exposures, there is temporary irritation of mucous membranes, headache, nausea, and, occasionally, permanent eye injuries. Skin application of BCME results in transient or permanent skin necrosis (dependent on dosage) in mice and skin irritation and corneal injury in rabbits (the lat-

ter finding does not necessarily imply absorption and systemic transfer but is more likely due to vaporization from the skin and a direct eye effect).

5. Carcinogenic effects: BCME is a potent carcinogen in rodents and humans, almost always at the site of application (fibrosarcomas on subcutaneous administration and skin tumors on skin application, pulmonary adenomas on inhalation in mice and rats); subcutaneous injection in newborn mice also results in lung adenomas. In humans, industrial exposure to BCME results in significant incidence of lung cancers.

6. Mutagenic and teratogenic effects: BCME is mutagenic in the Ames test and in E. coli. There is no evidence for teratogenicity.

Emergency Treatment

1. Skin and eye exposure: For skin exposure, remove contaminated clothing and wash skin with a mild soap and water. Rinse with water for at least five minutes. For eye exposure, irrigate immediately with copious quantities of running water for at least 15 minutes.

2. Ingestion: Administer an antacid preparation. Induce vomiting.

3. Inhalation: Remove victim promptly to clean air. Administer rescue breathing if necessary.

4. Refer to physician at once. Consider treatment for pulmonary irritation.

References

Althouse, R., J. Huff, L. Tomatis, and J. Wilbourn. 1980. An evaluation of chemicals and industrial processes associated with cancer in humans based on human and animal data: IARC Monographs Volumes 1 to 20: Report of an IARC Working Group. Cancer Res 40:1-12.

Alvarez, M., and R.T. Rosen. 1976. Formation and decomposition of bis(chloromethyl) ether in aqueous media. Int J Environ Anal Chem 4:241-246.

Collier, L. 1972. Determination of bis(chloromethyl) ether at the ppm level in air samples by high-resolution mass spectrometry. Environ Sci Technol 6:930-932.

Drew, R.T., S. Laskin, M. Kuschner, and N. Nelson. 1975. Inhalation carcinogenicity of alpha halo ethers. I. The acute inhalation toxicity of chloromethyl methyl ether and bis(chloromethyl) ether. Arch Environ Health 30:61-69.

Evans, K.P., A. Mathias, N. Mellor, R. Silvester, and A.E. Williams. 1975. Detection and estimation of bis(chloromethyl) ether in air by gas chromatography-high resolution mass spectrometry. Anal Chem 47:821-824.

Frankel, L.S., and R.F. Black. 1976. Automatic gas chromatographic

monitor for the determination of parts-per-billion levels of bis (chloromethyl) ether. Anal Chem 48:732-737.

Katayama, M., and Y. Morino. 1949. Raman spectra of monochloromethyl ether and 1,2-dichloromethyl ether. Reports Rad Chem Res Inst 4:1-2.

Pellizzari, E.E. 1974. Development of method for carcinogenic vapor analysis in ambient atmospheres. Office of Research and Development, U.S. Environmental Protection Agency, Washington, DC, EPA 650/2-74-121.

Shadoff, L.A., G.J. Kallos, and J.S. Woods. 1973. Determination of bis(chloromethyl) ether in air by gas chromatography-mass spectrometry. Anal Chem 45:2341-2344.

Solomon, R.A., and G.J. Kallos. 1975. Determination of chloromethyl methyl ether and bis-chloromethyl ether in air at the ppb level by gas-liquid chromatography. Anal Chem 47:955-957.

Tou, J.C., and G.J. Kallos. 1974. Kinetic study of the stabilities of chloromethyl methyl ether and bis(chloromethyl) ether in humid air. Anal Chem 46:1866-1869.

Tou, J.C., L.B. Westover, and L.F. Sonnabend. 1974. Kinetic studies of bis(chloromethyl) ether hydrolysis by mass spectrometry. J Phys Chem 78:1096-1098.

Van de Ven, L.G.J., and A. Venema. 1979. Determination of bis(chloromethyl) ether in air. Anal Chem 51:1016-1019.

Van Duuren, B.L., B.M. Goldschmidt, C. Katz, L. Langseth, G. Mercado, and A. Sivak. 1968. Alpha-halo ethers: A new type of alkylating carcinogen. Arch Environ Health 16:472-476.

Westover, L.B., J.C. Tou, and J.H. Mark. 1974. Novel mass spectrometric sampling device: Hollow fiber probe. Anal Chem 46:568-571.